Blood Vessel Model using Tissue Modules with on-demand Stimuli

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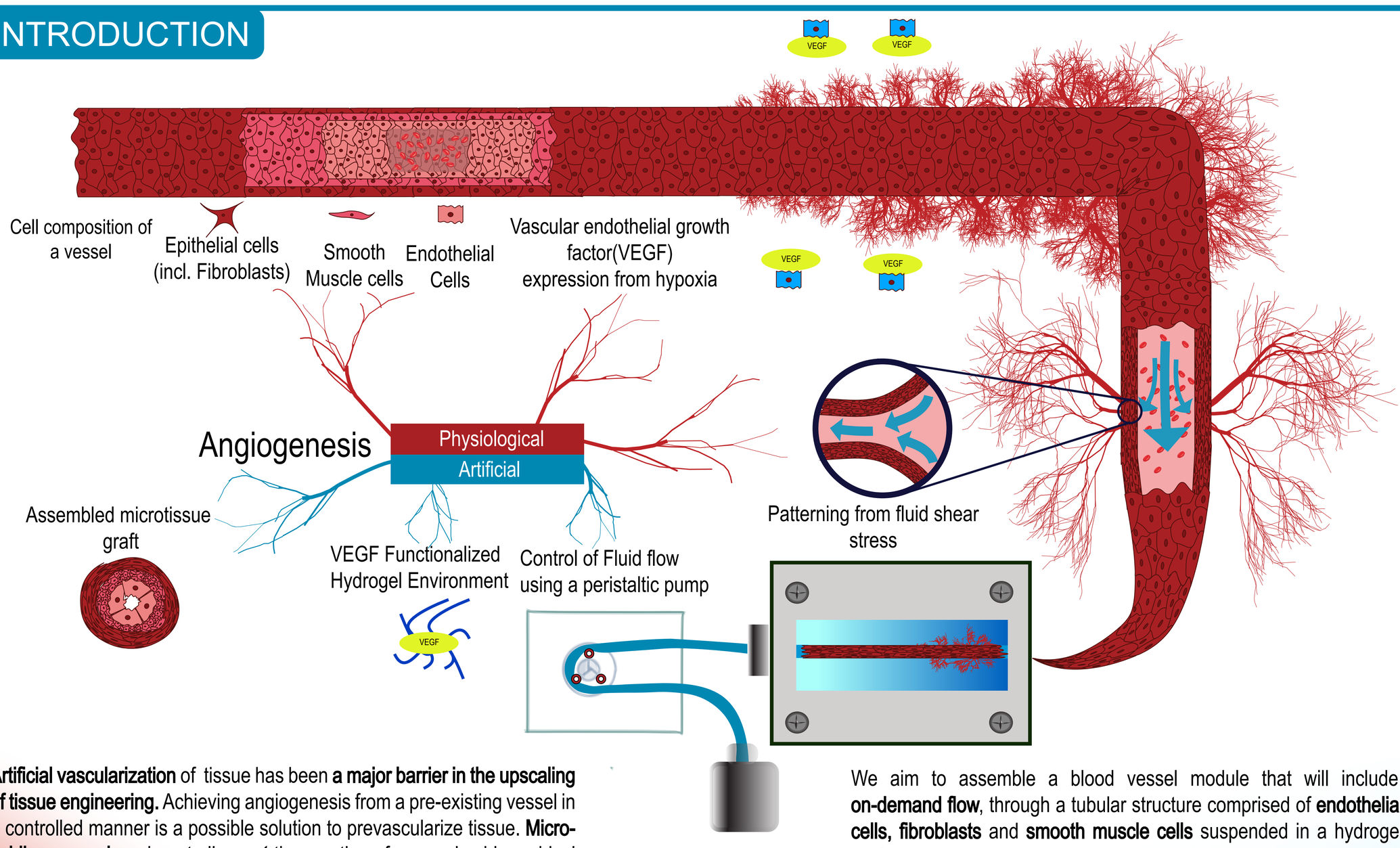
INTRODUCTION



Artificial vascularization of tissue has been **a major barrier in the upscaling of tissue engineering.** Achieving angiogenesis from a pre-existing vessel in a controlled manner is a possible solution to prevascularize tissue. **Micro-fluidic approaches** do not allow **yet** the creation of a complex hierarchical tissue construct that can be **manipulated and removed** from the creation template.Thus the challenge is to simulate angiogenesis in a **1:1 scale.**

CHALLENGE

We aim to assemble a blood vessel module that will include: **on-demand flow**, through a tubular structure comprised of **endothelial cells, fibroblasts** and **smooth muscle cells** suspended in a hydrogel environment **functionalized with growth factors**.

AIM

METHODS

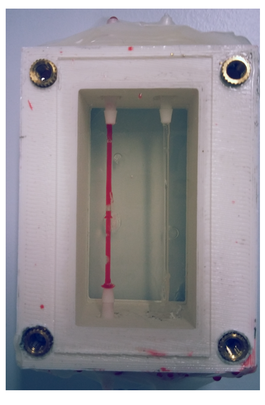
The module was created using a 3D bioprinter (ROKITINVIVO). For the fluidic mold Polylactic Acid filament (PLA 1.75 mm, 3D4MAKERS) was extruded at 230°C with a 200 μm nozzle at 10 mm/s. Microfluidic mount connectors (PMK210, Nordson) were attached to the designed threads in the fluidic mold. Next, a sacrificial tubular channel of Polyvinylalcohol (PVA) was printed separately and attached to the mount connectors. Glass microscopy slides were cut with a laser cutter to fit the top socket, and then they were secured by fusing the two lid components with acetone. Finally the fluidic mold was filled with Gelatin (Porcine Gelatin Type A) infused with VEGF-1 and put in the fridge at 4°C overnight. After assembling the construct, water flow was applied to dissolve the PVA and make a hollow channel.

RESULTS

The PLA fluidic mold printing process has been optimized in order to create a water tight connection with the mount connectors.
Channels of 600 μm diameter have been created within the Gelatin structure, by removing PVA with water. We have also shown that it is possible create channels by fitting two needles during the gelatin mold casting step as shown below **(Figures C,D)**

C

D



OUTLOOK

So far we have developed **a fluidic mold** that can be used for fabrication of the main **tissue block** functionalized with **VEGF**, as well as to provide fluid flow through vascular channel on-demand. The next step is creating the vascular graft and inserting it in the hollow channel. The first step is to seed endothelial cells and test our data collection potential **(Figure C)**. If successful, we will proceed with upscaling towards the microtissue graft. Furthermore the pathway of the PVA channel is **completely customizable** so we will be able to implement multiple channels with different architectures in proximity, observe the grafts interactions and try to simulate anastomosis **(Figure D)**.

C

D

ACKNOWLEDGEMENTS

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